

EXHIBIT 13



US006180337B1

(12) **United States Patent**
Caskey et al.

(10) **Patent No.:** **US 6,180,337 B1**
(45) **Date of Patent:** ***Jan. 30, 2001**

(54) **DIAGNOSIS OF THE FRAGILE X SYNDROME**

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(*) Notice: Under 35 U.S.C. 154(b), the term of this patent shall be extended for 0 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **07/751,891**

(22) Filed: **Aug. 29, 1991**

Related U.S. Application Data

(63) Continuation-in-part of application No. 07/705,490, filed on May 24, 1991.

(51) Int. Cl.⁷ **C12Q 1/68**; G01N 33/53; C07H 21/02; C07K 14/435

(52) U.S. Cl. **435/6**; 435/7.1; 435/91.2; 536/23.5; 536/24.33; 530/350

(58) Field of Search 435/6, 91.2; 536/27, 536/23.1, 23.5, 24.33; 530/350; 935/77, 78

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Primary Examiner—Stephanie Zitomer

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(57) **ABSTRACT**

A sequence of the FMR-1 gene is disclosed. This sequence and related probes, cosmid and unique repeats are used to detect X-linked diseases and especially the fragile X syndrome. Also, methods using methylation-sensitive restriction endonuclease and PCR primer probes were used to detect X-linked disease.

9 Claims, 15 Drawing Sheets

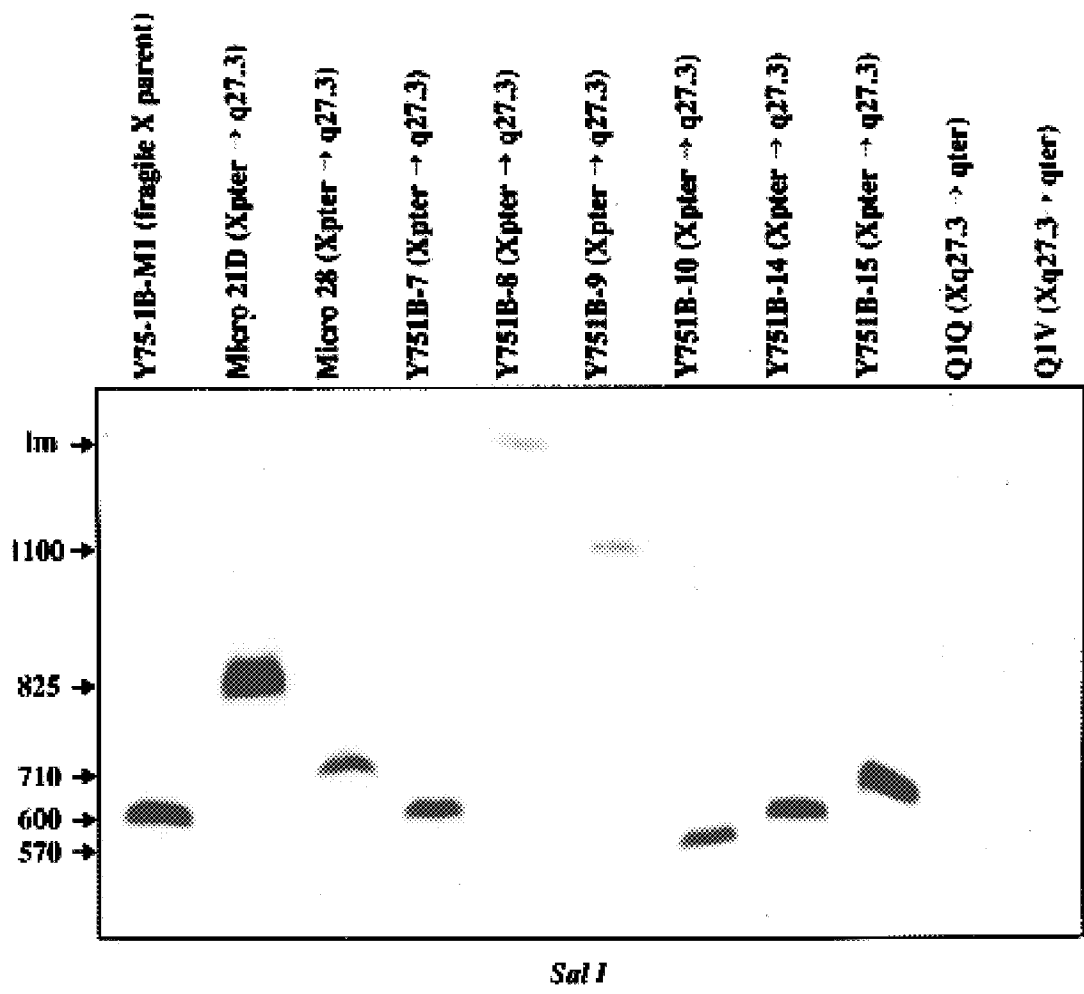


Figure 1

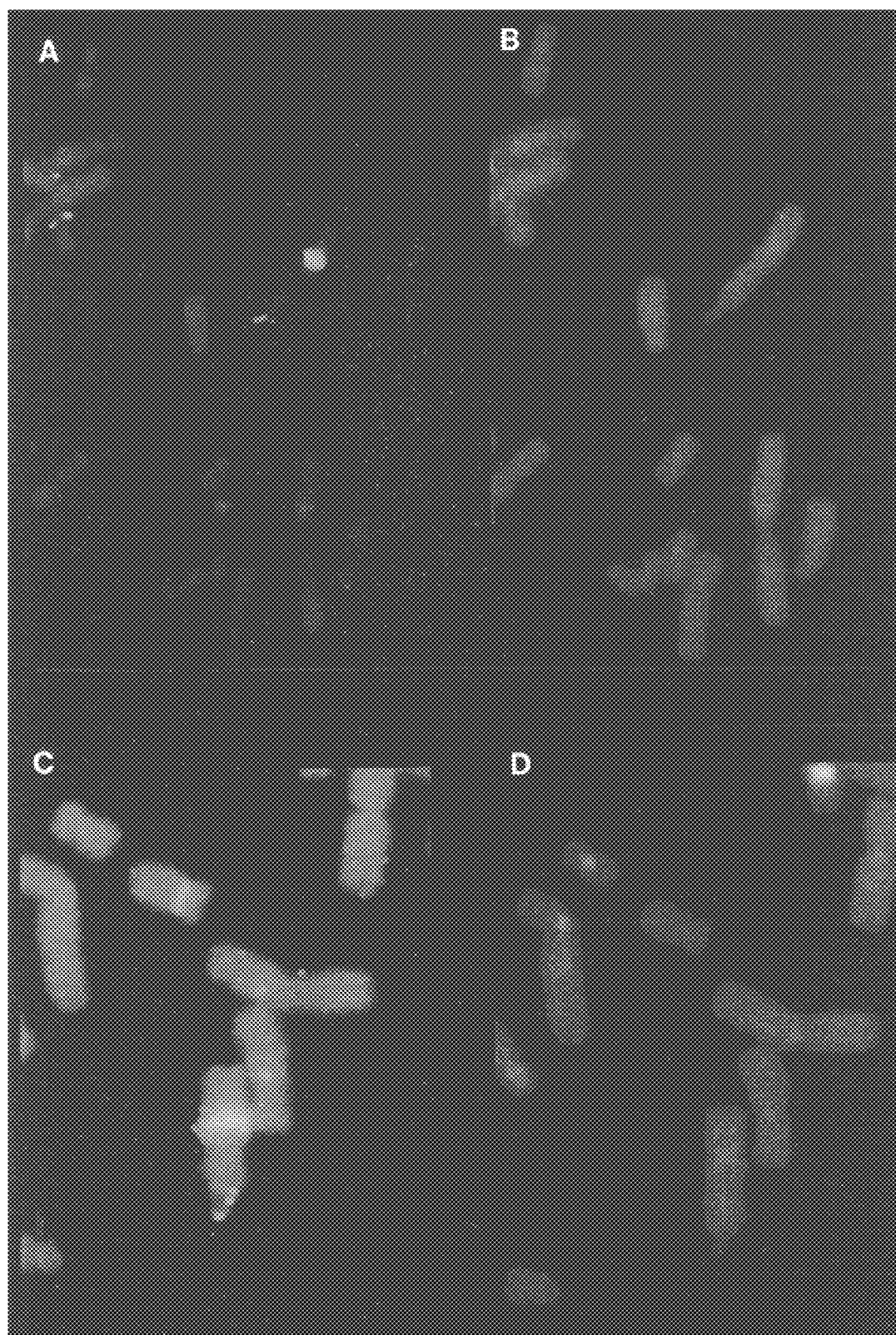


Figure 2

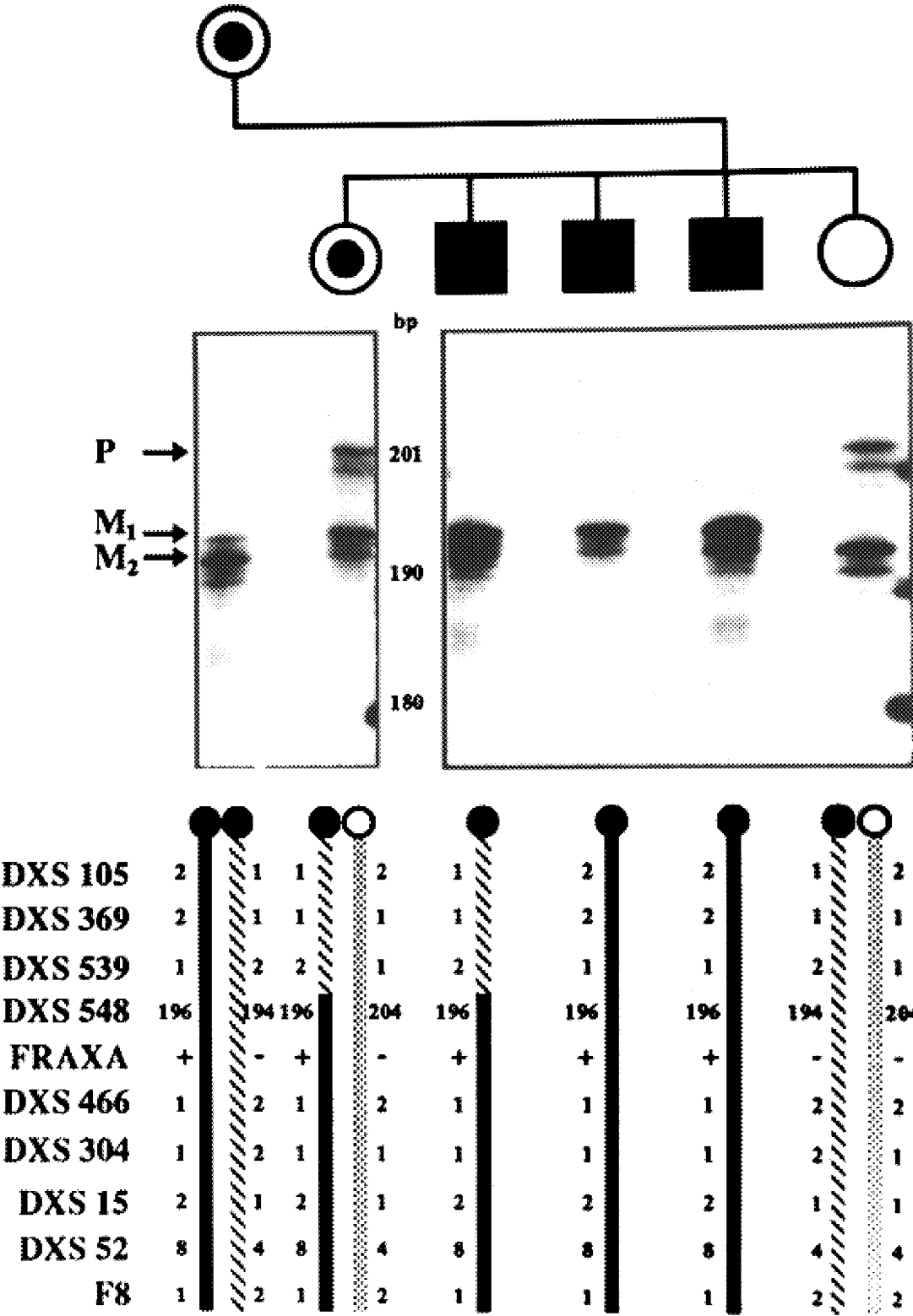


Figure 3

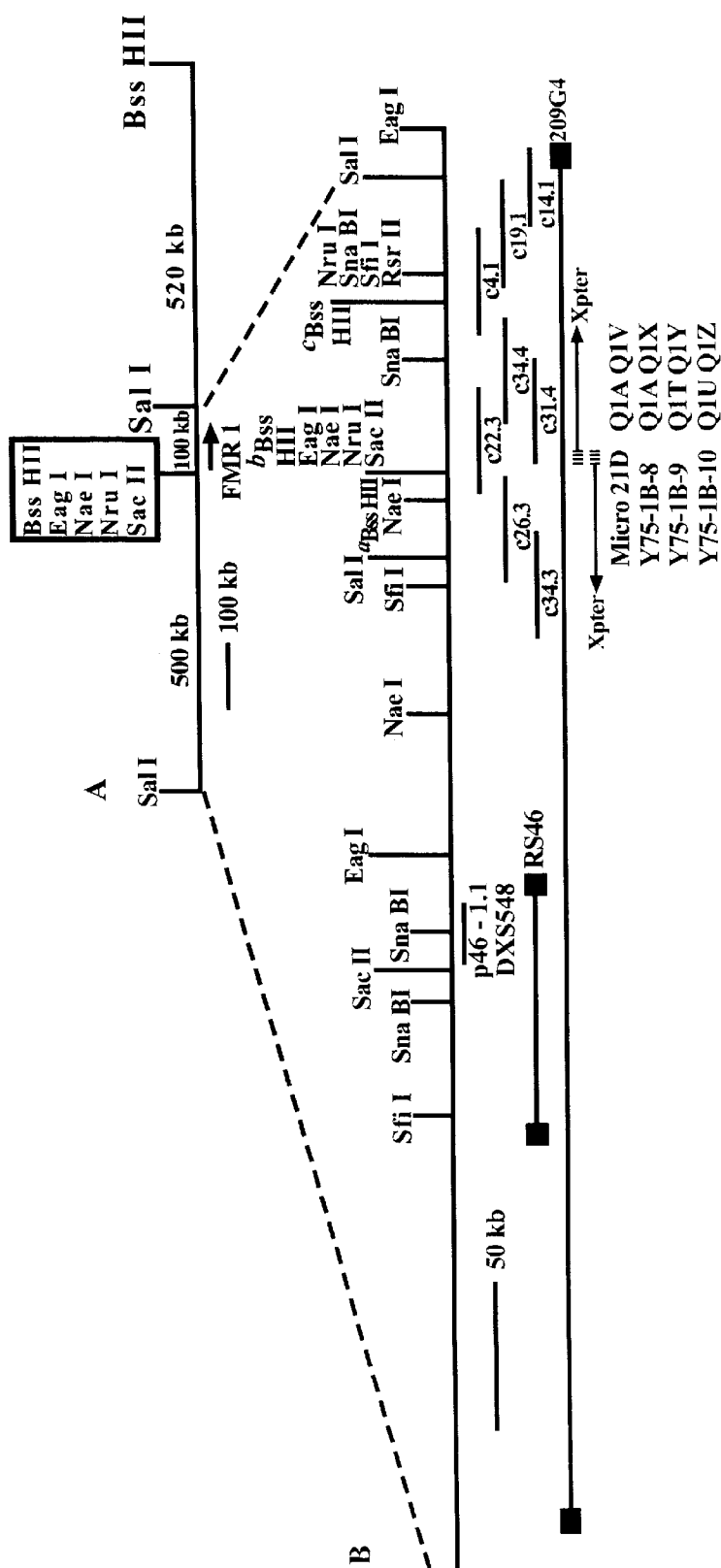


Figure 4

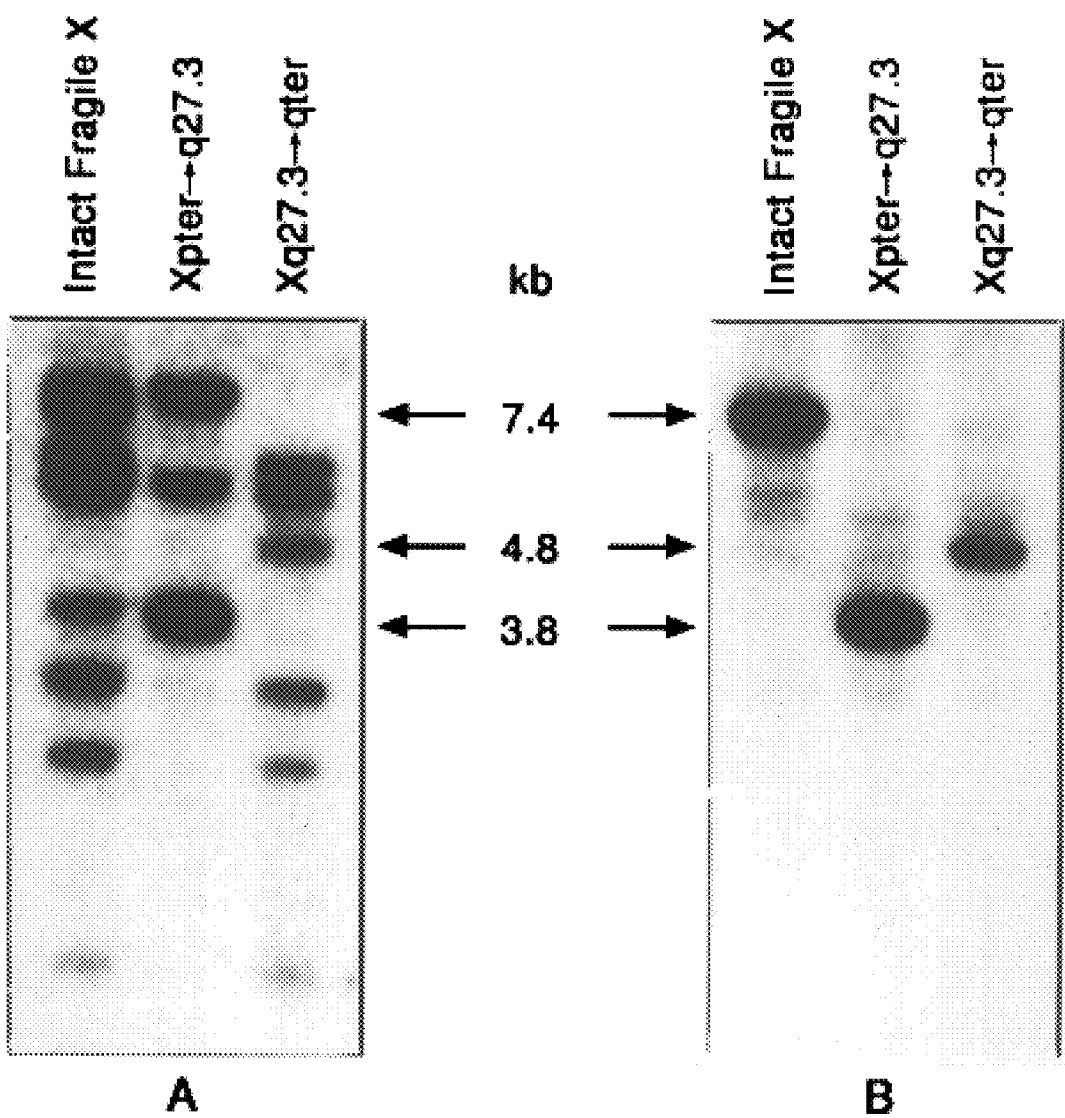


Figure 5

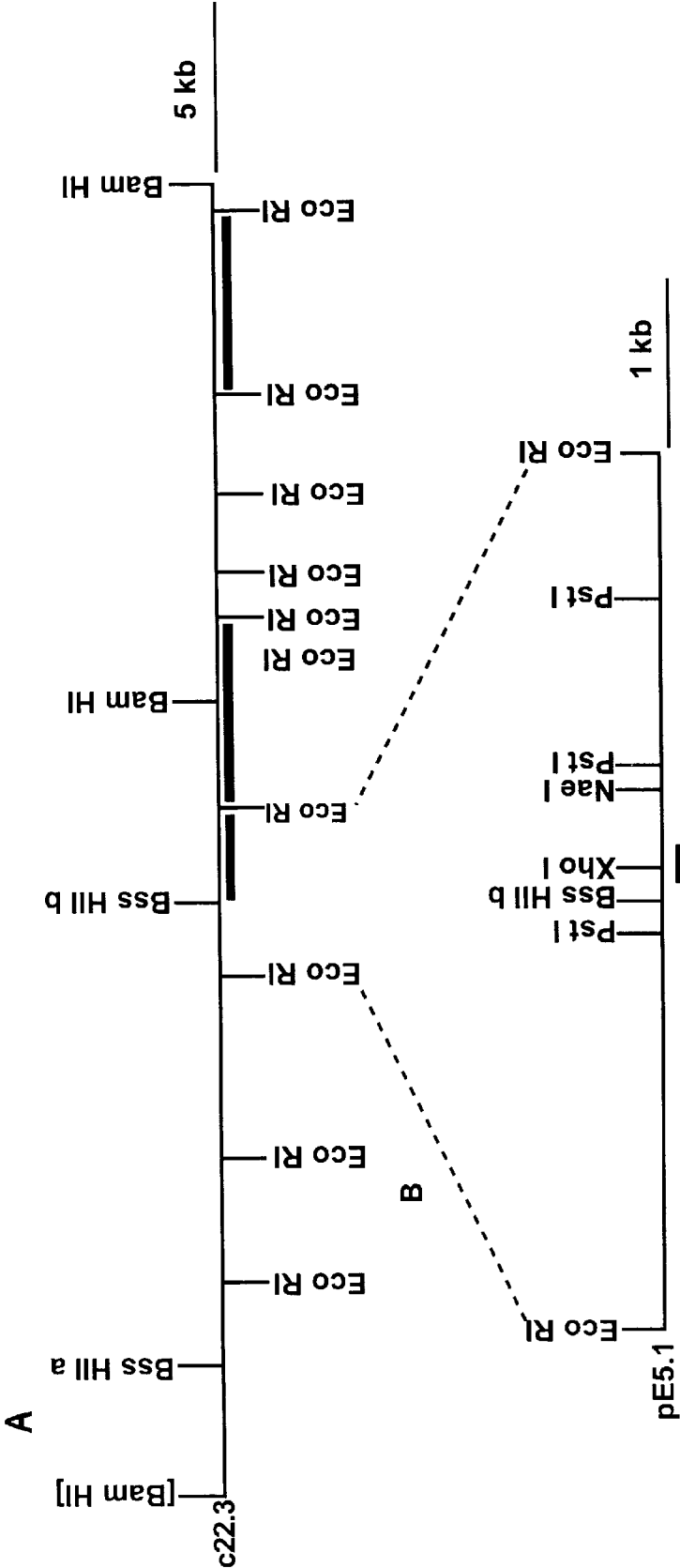


Figure 6

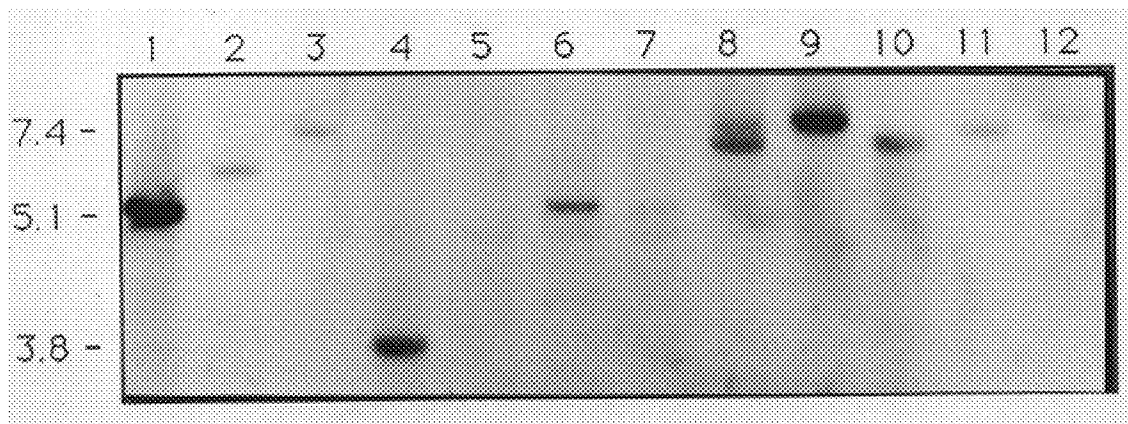


Figure 7

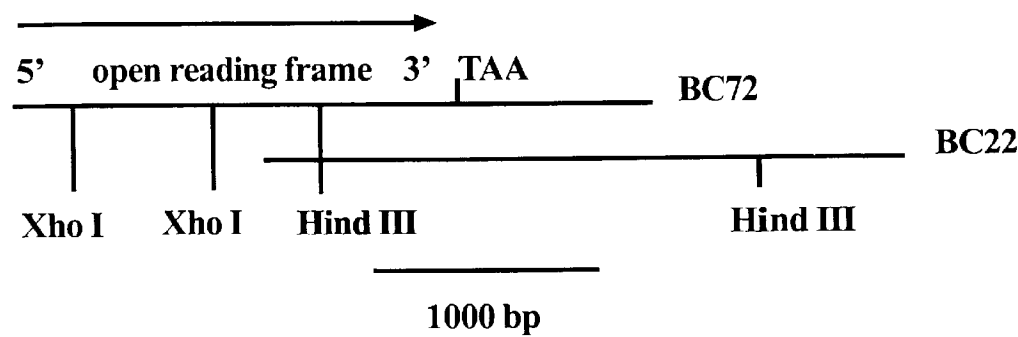


Figure 8

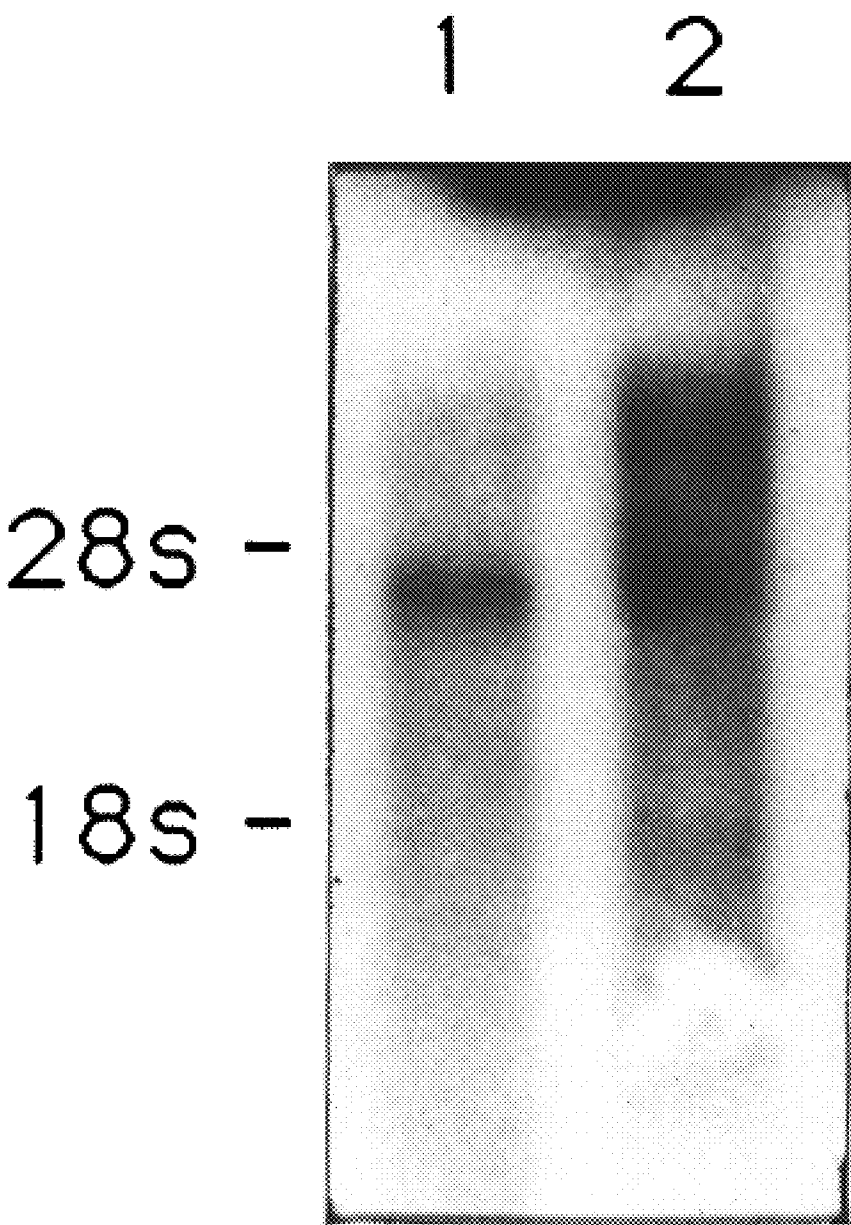


Figure 9

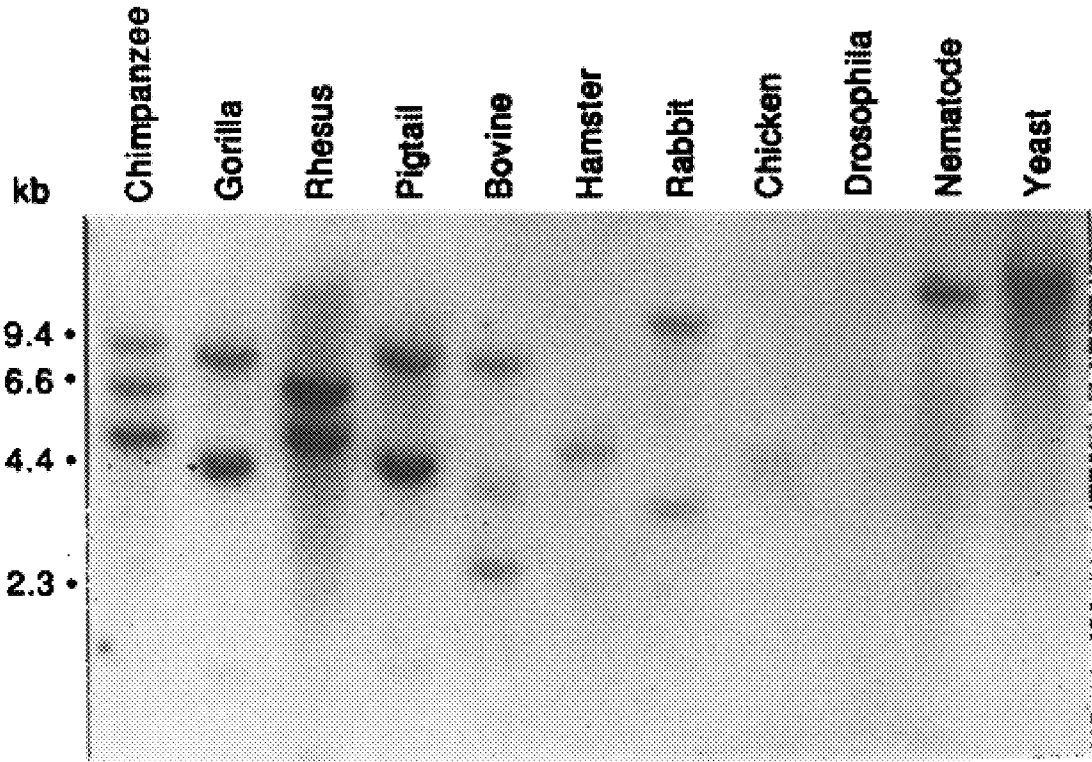


Figure 10

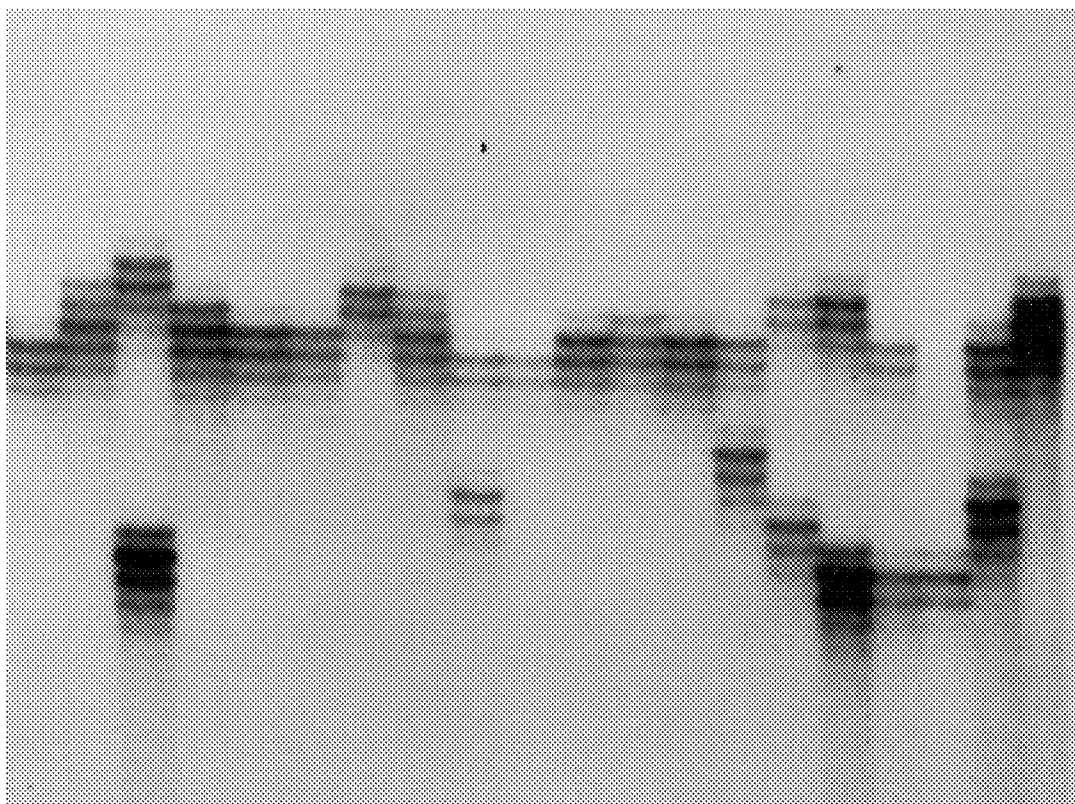


Figure 12

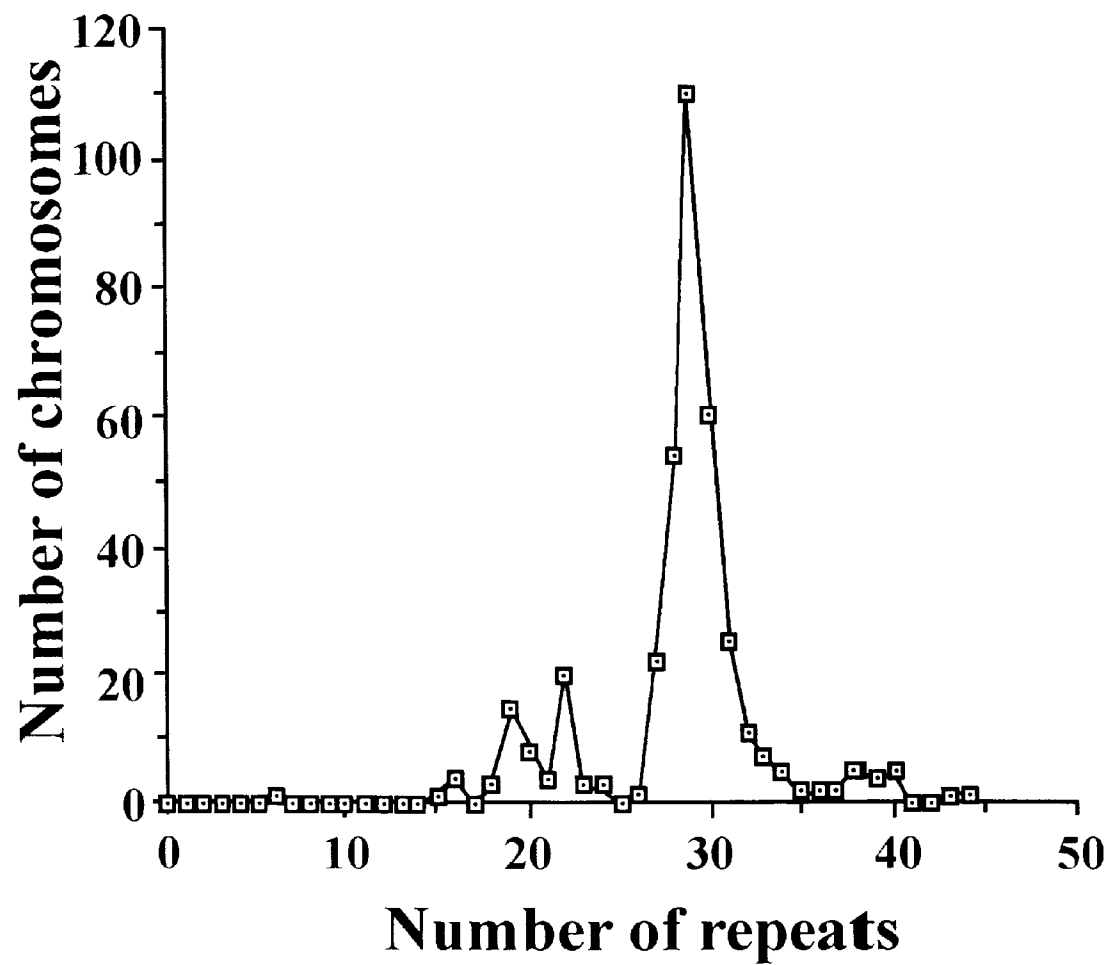


Figure 13

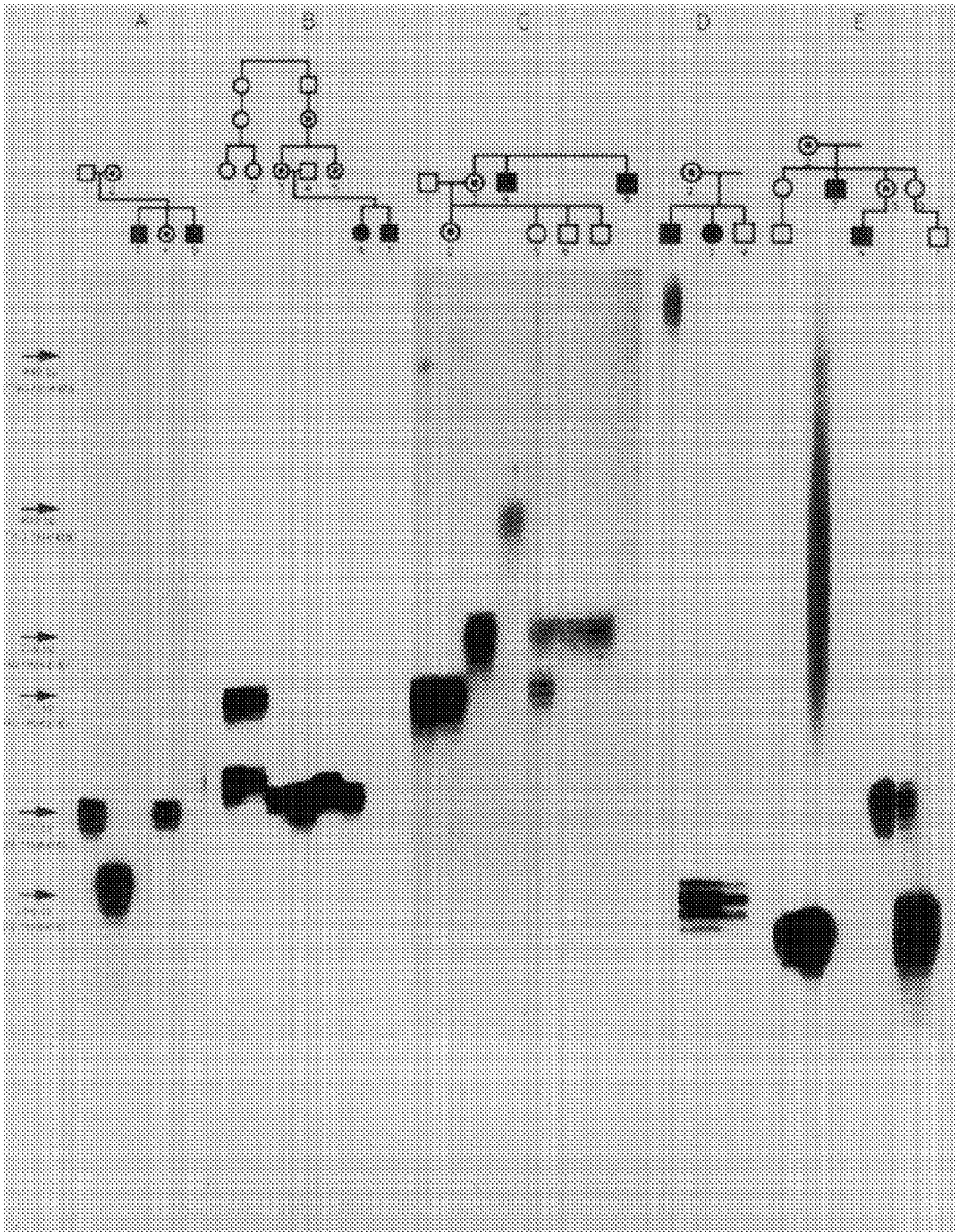


Figure 14

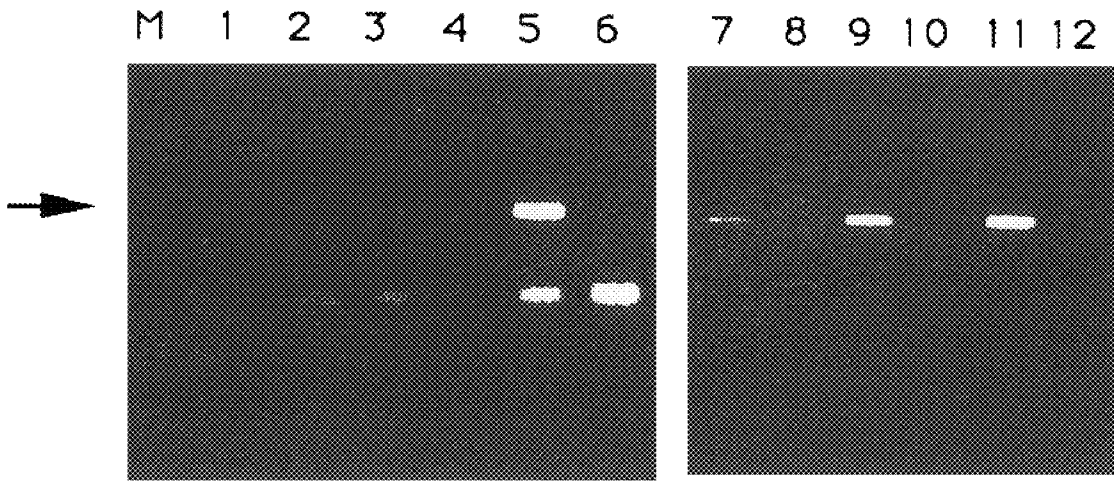


Figure 15